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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/805,650	03/19/2004	Michael Borns	25436/2382	9645

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PALMER & DODGE, LLP
KATHLEEN M. WILLIAMS / STR
111 HUNTINGTON AVENUE
BOSTON, MA 02199

EXAMINER	
STAPLES, MARK	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 12/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/805,650	BORNS, MICHAEL	
	Examiner	Art Unit	
	Mark Staples	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/19/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *12, 14, 16-18, 20-24, and 31-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, 13, 15, 19, and 25-30* is/are rejected.

7)☒ Claim(s) *3, 7, and 9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/08/2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/23/04 & 12/28/04*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20061106*; 11/15/06
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-30, in the reply filed on October 19, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, this election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 31-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on October 19, 2006.

2. Applicant's election with traverse of Subgroup Pfu (wild type)-Sso7d fusion, for example the nucleotide sequence SEQ ID NO. 126 and amino acid sequence SEQ ID NO. 127, in the reply filed on October 19, 2006 is acknowledged. It is noted that this election was clarified in telephone discussions from 11/06/2006 to 11/15/2006 which are summarized in the Interview Summary which accompanies this action. It is further noted that SEQ ID NO. 126 and SEQ ID NO. 127 are not recited in the claims. Thus the elected claims recite any fusion of Pfu (wild type) to Sso7d protein including the fusion identified by SEQ ID NOs. 126 and 127. The traversal is on the ground(s) that the subgroups of Group I are not patentably distinct and are obvious variants, since each subgroup exhibits the identical property of increased processivity.

This is not found persuasive because the processivity cited as an identical property is in fact a property which is specific, and thus non-identical, to each of the subgroups. The processivity increases are for specific enzymatic activities and sometimes require specific substances being present as well. The subgroup of the helix-hairpin-helix DNA binding motifs from DNA topoisomerase V and DNA polymerase fusion increase polymerase processivity. The subgroup of thioredoxin binding domain and T7 DNA polymerase fusion increases T7 DNA polymerase processivity in the presence of thioredoxin. The subgroup of archael PCNA binding domain and Taq DNA polymerase fusion increases Taq DNA polymerase processivity in the presence of PCNA. The subgroup of Pfu DNA polymerase and binding protein Sso7d increases the processivity of the Pfu polymerase. These different processivities are disclosed in the instant application, see paragraph 1 on page 3.

Furthermore, an increase in processivity is not an intrinsic property of a polymerase-partner fusion. Wang (2001) teaches an example of a polymerase-peptide PL-ΔTaq fusion which shows decreased processivity over the unmodified polymerase, Taq (see p. 35, 3rd paragraph). Thus having a fusion product is not predictive, by itself, of increased processivity. Thus each subgroup has to be examined separately to ascertain whether the claimed increase in processivity is supported by the disclosure.

Additionally, each of the fusion subgroups have different nucleotide and amino acid sequences and thus each is a patentably distinct structure. Each structure requires its own separate search in multiple databases. Searching all the subgroups claimed would be a serious search burden.

The Subgroup election requirement is still deemed proper and is therefore made FINAL.

Claims 12, 14, 16-18, and 20-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subgroup, there being no allowable generic or linking claim. Claims 12, 14, 16-18, and 20-24 recite substitutions and mutations of the wild type Pfu polymerase and thus these claims do not recite the elected subgroup of wild type Pfu fused to Sso7d protein. Applicant timely traversed the Subgroup restriction (election) requirement in the reply filed on October 19, 2006.

In summary, claims 1-11, 13, 15, 19, 25, 26, 28 and 29 of Group 1 as filed on October 19, 2006 will be fully examined for patentability. Claims 27 and 30 as filed on October 19, 2006 will be examined only to the extent that they incorporate the elected subgroup Pfu (wild type)-Sso7d fusion.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

4. The use of the trademarks VENT® and DEEPVENT® have been noted in this application. They and any other trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

5. Claim 3 is objected to because of the following informalities: a period is missing at the end of this claim. Appropriate correction is required.

6. Claims 7 and 9 are objected to because of the following informalities: these claims recite the plural "steps" when only a single active "step" of "incubating" is given. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 27 contains the trademark/trade names VENT® and DEEPVENT®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the

requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe "proofreading polymerase" and, accordingly, the identification/description is indefinite.

For clarity, it is noted that Pfu is not a trademark name, it is an abbreviation for the native enzyme, DNA polymerase of *Pyrococcus furiosus*, a hyperthermophillic archaebacterium. Also, KOD is not a trademark named, it is an abbreviation for the recombinant form of *Thermococcus kodakaraensis* KOD1 DNA polymerase. And Tgo is not a trademark name, it is an abbreviation for the DNA polymerase isolated from *Thermococcus gorgonarius*.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: synthesizing DNA as recited in the preamble.

Specifically, the preamble of the method recites that the method is for DNA synthesis, but the final active recited step is, "contacting said fusion with a nucleic acid template." The phrase, "wherein said fusion permits DNA synthesis," is not recited in a

positive fashion and the word, "permits" also renders the claim confusing in whether the synthesis is actually occurring or the phrase is further describing the polymerase.

Claim 5 recites the limitation " said first DNA molecule " in line 6. There is insufficient antecedent basis for this limitation in the claim.

The term " high pH " in claims 1-11, 13, 15-16, 19-20, and 25-30 is a relative term which renders the claim indefinite. The term " high pH " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, for a reaction requiring an acidic condition (i.e., pH of 2), pH 3 would be considered high. However, for a reaction requiring a basic condition (i.e., pH of 9), then pH 3 would no longer be considered high.

The term "reduced" in claims 11, 13, 15, 16, 19, and 20 is a relative term which renders the claims indefinite. The term "reduced" is not defined by the claim relative to anything, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what “reduced” is relative to, whether it might be to polymerase-protein fusion activity of an antecedent claim, or to the non-fused polymerase activity of an antecedent claim, or to some other activity. The use of the term “reduced” thus renders the “activity” of the claims indefinite.

Claims 1-11, 13, 15-16, 19-20, and 25-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11, 13, 15-16, 19-20, and 25-30 are indefinite for the recitation of the term "DNA polymerase fusion" because the term "fusion" connotes that the polymerase is "fused" with another molecule, but the claim fails to recite what the molecule is nor does the claim define the fusion in terms of its function, rendering the claim indefinite in its metes and bounds.

Claim 15 is indefinite for reciting the phrase, "said DNA polymerase has reduced base analog detection activity" because it is unclear whether this limitation is a further limitation to its parent claim which recites that the DNA polymerase has a reduced polymerization activity.

Claim 7 is indefinite for reciting the phrase, "under conditions" because it is unclear whether these conditions refer to a fusion of a mutated polymerase or other mutated protein, or whether the conditions refer to amplification parameters such as time or temperature, or whether the conditions refer to something else. The conditions are not defined and hence it is unclear what conditions are needed for the claimed method of producing a mutated amplified product.

Claim 9 is indefinite for reciting the phrase, "under conditions" because it is unclear whether these conditions refer to a fusion of a reverse transcriptase, or whether the conditions refer to amplification parameters such as time or temperature, or whether

the conditions refer to something else. The conditions are not defined and hence it is unclear what conditions are needed for the claimed method of reverse transcriptase PCR.

Claims 11, 13, 15, 16, 19, and 20 are indefinite for reciting the phrase, "reduced . . . activity" because it is unclear how this reduction is accomplished. The claims do not provide steps, conditions, or instructions on how the "reduced . . . activity" is accomplished.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 13, 15, 19, and 25-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The current claims recite methods comprising a DNA polymerase fusion, consisting of a DNA polymerase and one or more fusion partners set forth in the independent claims 1, 3, 5, 7, and 9. The word, "fusion" is described as, "a first amino acid sequence (protein) comprising a wild type or mutant DNA polymerase of the invention, joined to a second amino acid sequence defining a polypeptide that modulates one or more activities of the DNA polymerase including but not limited to,

processivity, salt-resistance, DNA binding, strand displacement activity, polymerase activity, nucleotide binding and recognition, 3'-5' or 5' to 3' exonuclease activities..." (page 8). Since this definition is "not limited to" the listed subgroups, the claims broadly recite fusions consisting of any DNA polymerase with any amino acid sequence (which includes the minimum of a dipeptide) which modulates any activity of the DNA polymerase. Since any modification of a DNA polymerase is expected to modulate some activity of the polymerase, such as the diffusion rate which should decrease with increased size, the claims as recited encompass a fusion to any peptide, polypeptide, or protein. It is noted that the definition does not disclose that the modulation be beneficial for DNA synthesis, nor does the modulation have to affect the polymerase activity. Furthermore the claims broadly recite that not only can any naturally occurring (wild type) polymerase can be fused and used in the methods but also that any mutant polymerase can be fused and used in the methods. The mutations are not limited in the definition and thus include insertions, deletions, and substitutions. While applicant only discloses one example, Example 3, which uses the methods as claimed; the claims broadly encompasses hundreds of millions of different possibilities for DNA polymerase fusions and thus encompasses hundreds of millions of different possibilities for methods using DNA polymerase fusions.

Furthermore, no common elements or attributes of the variants as set forth in the independent claims 1, 3, 5, 7, and 9 are disclosed. With regard to the various peptides, polypeptides and proteins, the example given is insufficient to demonstrate identity of all specific fusions of the claimed invention. The instant claims are overly broad in the recitation of "providing" or "contacting . . . with" a DNA polymerase fusion, since no guidance is provided as to which of the variant fusions would retain or have the claimed

polymerase activity necessary for DNA synthesis. Further no information is given in the specification regarding a methodology to determine such common elements or attributes.

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that "...if inventor is unable to envision detailed chemical structure, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after the compound has been isolated.

In the application at the time of filing, there is no record or description which would demonstrate conception or written description of the multitude of claimed DNA fusions.

Accordingly, the specification does not provide a written description of the invention of claims 1-11, 13, 15, 19, and 25-30.

Table 1 is given below for discussion which follows it.

Table 1

Pfu (wild type) – Sso7d Fusion

Application	10805650
Search Result	20061122_074851_us-10-805-650-126.gap0.1.rng.
Title:	US-10-805-650-126
Perfect score:	2481
Sequence:	1 atgattttagatgtggatta.....tggagaagcagaaaaagtga 2481

Nucleotide Match of SEQ ID NO. 7 to SEQ ID NO. 126 of instant application

```
RESULT 1

AAD24821
ID   AAD24821 standard; DNA; 2535 BP.
XX
AC   AAD24821;
XX
DT   29-AUG-2003  (revised)
DT   12-MAR-2002  (first entry)
XX
DE   Pyrococcus furiosus Pfu - Sulfolobus solfataricus Sso7d fusion DNA.
XX
KW   Nucleic acid modifying enzyme; nucleic-acid-binding domain; Sac7d; Sso7d;
KW   PolI DNA polymerase; Pfu DNA polymerase; ds.
XX
OS   Pyrococcus furiosus.
OS   Sulfolobus solfataricus.
OS   Chimeric.
XX
FH   Key             Location/Qualifiers
FT   CDS             1. .2535
FT                   /*tag=  a
FT                   /product= "Pfu-Sso7d fusion protein"
XX
PN   WO200192501-A1.
XX
PD   06-DEC-2001.
```

Table 1 continued

```
XX
PF   29-MAY-2001; 2001WO-US017492.
XX
PR   26-MAY-2000; 2000US-0207567P.
PR   16-AUG-2000; 2000US-00640958.
XX
PA   (MJBI-) MJ BIOWORKS INC.
XX
PI   Wang Y;
DR   WPI; 2002-075467/10.
DR   P-PSDB; AAE15567.
XX
PT   Protein for nucleic acid modification, consists of a heterologous
PT   sequence-non-specific double-stranded nucleic-acid-binding domain joined
PT   to a heterologous catalytic nucleic-acid-modifying domain.
XX
PS   Example 1; Page 47-48; 65pp; English.
XX
CC   The invention relates to improved generation of nucleic acid modifying
CC   enzymes. The improvement is the fusion of a sequence-non-specific double-
CC   stranded nucleic-acid-binding domain to the enzyme in a manner that
CC   enhances the ability of the enzyme to bind and catalytically modify the
CC   nucleic acid. The sequence-non-specific nucleic-acid-binding domain can
CC   specifically bind to polyclonal antibodies generated against either Sac7d
CC   or Sso7d. Protein consisting of heterologous sequence-non-specific double
CC   -stranded nucleic-acid-binding domain joined to heterologous catalytic
CC   nucleic-acid-modifying domain is useful for modifying a nucleic acid in
CC   an aqueous solution. The proteins of the invention are useful for
CC   amplifying a subsequence of a target nucleic acid using a polymerase
CC   chain reaction (PCR). The present sequence is Pyrococcus furiosus PolI
CC   DNA polymerase (Pfu) - Sulfolobus solfataricus Sso7d fusion DNA. (Updated
CC   on 29-AUG-2003 to standardise OS field)
XX
SQ   Sequence 2535 BP; 924 A; 408 C; 621 G; 582 T; 0 U; 0 Other;

  Query Match             99.6%;  Score 2471;  DB 6;  Length 2535;
  Best Local Similarity   97.9%;  Pred. No. 1.9e-167;
  Matches 2481;  Conservative    0;  Mismatches    0;  Indels   54;  Gaps
1;

Qy          1 ATGATTTTAGATGTGGATTACATAACTGAAGAAGGAAAACCTGTTATTAGGCTATTCAAA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 ATGATTTTAGATGTGGATTACATAACTGAAGAAGGAAAACCTGTTATTAGGCTATTCAAA 60

Qy         61 AAAGAGAACGGAAAATTTAAGATAGAGCATGATAGAACTTTTAGACCATACATTTACGCT 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 AAAGAGAACGGAAAATTTAAGATAGAGCATGATAGAACTTTTAGACCATACATTTACGCT 120

Qy        121 CTTCTCAGGGATGATTCAAAGATTGAAGAAGTTAAGAAAATAACGGGGGAAAGGCATGGA 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 CTTCTCAGGGATGATTCAAAGATTGAAGAAGTTAAGAAAATAACGGGGGAAAGGCATGGA 180
```

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Qy        181 AAGATTGTGAGAATTGTTGATGTAGAGAAGGTTGAGAAAAAGTTTCTCGGCAAGCCTATT 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 AAGATTGTGAGAATTGTTGATGTAGAGAAGGTTGAGAAAAAGTTTCTCGGCAAGCCTATT 240

Qy        241 ACCGTGTGGAAACTTTATTTGGAACATCCCCAAGATGTTCCCACTATTAGAGAAAAAGTT 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 ACCGTGTGGAAACTTTATTTGGAACATCCCCAAGATGTTCCCACTATTAGAGAAAAAGTT 300

Qy        301 AGAGAACATCCAGCAGTTGTGGACATCTTCGAATACGATATTCCATTTGCAAAGAGATAC 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 AGAGAACATCCAGCAGTTGTGGACATCTTCGAATACGATATTCCATTTGCAAAGAGATAC 360

Qy        361 CTCATCGACAAAGGCCTAATACCAATGGAGGGGGAAGAAGAGCTAAAGATTCTTGCCTTC 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 CTCATCGACAAAGGCCTAATACCAATGGAGGGGGAAGAAGAGCTAAAGATTCTTGCCTTC 420

Qy        421 GATATAGAAACCCTCTATCACGAAGGAGAAGAGTTTGGAAAAGGCCCAATTATAATGATT 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 GATATAGAAACCCTCTATCACGAAGGAGAAGAGTTTGGAAAAGGCCCAATTATAATGATT 480

Qy        481 AGTTATGCAGATGAAAATGAAGCAAAGGTGATTACTTGGAAAAACATAGATCTTCCATAC 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 AGTTATGCAGATGAAAATGAAGCAAAGGTGATTACTTGGAAAAACATAGATCTTCCATAC 540

Qy        541 GTTGAGGTTGTATCAAGCGAGAGAGAGATGATAAAGAGATTTCTCAGGATTATCAGGGAG 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 GTTGAGGTTGTATCAAGCGAGAGAGAGATGATAAAGAGATTTCTCAGGATTATCAGGGAG 600

Qy        601 AAGGATCCTGACATTATAGTTACTTATAATGGAGACTCATTCGACTTCCCATATTTAGCG 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 AAGGATCCTGACATTATAGTTACTTATAATGGAGACTCATTCGACTTCCCATATTTAGCG 660

Qy        661 AAAAGGGCAGAAAAACTTGGGATTAAATTAACCATTGGAAGAGATGGAAGCGAGCCCAAG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 AAAAGGGCAGAAAAACTTGGGATTAAATTAACCATTGGAAGAGATGGAAGCGAGCCCAAG 720

Qy        721 ATGCAGAGAATAGGCGATATGACGGCTGTAGAAGTCAAGGGAAGAATACATTTCGACTTG 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 ATGCAGAGAATAGGCGATATGACGGCTGTAGAAGTCAAGGGAAGAATACATTTCGACTTG 780

Qy        781 TATCATGTAATAACAAGGACAATAAATCTCCCAACATACACACTAGAGGCTGTATATGAA 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 TATCATGTAATAACAAGGACAATAAATCTCCCAACATACACACTAGAGGCTGTATATGAA 840

Qy        841 GCAATTTTTGGAAAGCCAAAGGAGAAGGTATACGCCGACGAGATAGCAAAAGCCTGGGAA 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 GCAATTTTTGGAAAGCCAAAGGAGAAGGTATACGCCGACGAGATAGCAAAAGCCTGGGAA 900

Qy        901 AGTGGAGAGAACCTTGAGAGAGTTGCCAAATACTCGATGGAAGATGCAAAGGCAACTTAT 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 AGTGGAGAGAACCTTGAGAGAGTTGCCAAATACTCGATGGAAGATGCAAAGGCAACTTAT 960
```

Table 1 continued

```
Qy       961 GAACTCGGGAAAGAATTCCTTCCAATGGAAATTCAGCTTTCAAGATTAGTTGGACAACCT
1020
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       961 GAACTCGGGAAAGAATTCCTTCCAATGGAAATTCAGCTTTCAAGATTAGTTGGACAACCT
1020

Qy      1021 TTATGGGATGTTTCAAGGTCAAGCACAGGGAACCTTGTAGAGTGGTTCTTACTTAGGAAA
1080
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1021 TTATGGGATGTTTCAAGGTCAAGCACAGGGAACCTTGTAGAGTGGTTCTTACTTAGGAAA
1080

Qy      1081 GCCTACGAAAGAAACGAAGTAGCTCCAAACAAGCCAAGTGAAGAGGAGTATCAAAGAAGG
1140
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1081 GCCTACGAAAGAAACGAAGTAGCTCCAAACAAGCCAAGTGAAGAGGAGTATCAAAGAAGG
1140

Qy      1141 CTCAGGGAGAGCTACACAGGTGGATTCGTTAAAGAGCCAGAAAAGGGGTTGTGGGAAAAC
1200
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1141 CTCAGGGAGAGCTACACAGGTGGATTCGTTAAAGAGCCAGAAAAGGGGTTGTGGGAAAAC
1200

Qy      1201 ATAGTATACCTAGATTTTAGAGCCCTATATCCCTCGATTATAATTACCCACAATGTTTCT
1260
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1201 ATAGTATACCTAGATTTTAGAGCCCTATATCCCTCGATTATAATTACCCACAATGTTTCT
1260

Qy      1261 CCCGATACTCTAAATCTTGAGGGATGCAAGAACTATGATATCGCTCCTCAAGTAGGCCAC
1320
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1261 CCCGATACTCTAAATCTTGAGGGATGCAAGAACTATGATATCGCTCCTCAAGTAGGCCAC
1320

Qy      1321 AAGTTCTGCAAGGACATCCCTGGTTTTATACCAAGTCTCTTGGGACATTTGTTAGAGGAA
1380
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1321 AAGTTCTGCAAGGACATCCCTGGTTTTATACCAAGTCTCTTGGGACATTTGTTAGAGGAA
1380

Qy      1381 AGACAAAAGATTAAGACAAAAATGAAGGAAACT--------------------------
1413
            ||||||||||||||||||||||||||||||||
Db      1381 AGACAAAAGATTAAGACAAAAATGAAGGAAACTCAAGATCCTATAGAAAAAATACTCCTT
1440
```

Table 1 continued

```
Qy       1414 ----------------------------TTAGCAAATTCTTTCTACGGATATTATGGCTAT
1446
                                            ||||||||||||||||||||||||||||||||||
Db       1441 GACTATAGACAAAAAGCGATAAAACTCTTAGCAAATTCTTTCTACGGATATTATGGCTAT
1500

Qy       1447 GCAAAAGCAAGATGGTACTGTAAGGAGTGTGCTGAGAGCGTTACTGCCTGGGGAAGAAAG
1506
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 GCAAAAGCAAGATGGTACTGTAAGGAGTGTGCTGAGAGCGTTACTGCCTGGGGAAGAAAG
1560

Qy       1507 TACATCGAGTTAGTATGGAAGGAGCTCGAAGAAAAGTTTGGATTTAAAGTCCTCTACATT
1566
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 TACATCGAGTTAGTATGGAAGGAGCTCGAAGAAAAGTTTGGATTTAAAGTCCTCTACATT
1620

Qy       1567 GACACTGATGGTCTCTATGCAACTATCCCAGGAGGAGAAAGTGAGGAAATAAAGAAAAAG
1626
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 GACACTGATGGTCTCTATGCAACTATCCCAGGAGGAGAAAGTGAGGAAATAAAGAAAAAG
1680

Qy       1627 GCTCTAGAATTTGTAAAATACATAAATTCAAAGCTCCCTGGACTGCTAGAGCTTGAATAT
1686
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 GCTCTAGAATTTGTAAAATACATAAATTCAAAGCTCCCTGGACTGCTAGAGCTTGAATAT
1740

Qy       1687 GAAGGGTTTTATAAGAGGGGATTCTTCGTTACGAAGAAGAGGTATGCAGTAATAGATGAA
1746
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 GAAGGGTTTTATAAGAGGGGATTCTTCGTTACGAAGAAGAGGTATGCAGTAATAGATGAA
1800

Qy       1747 GAAGGAAAAGTCATTACTCGTGGTTTAGAGATAGTTAGGAGAGATTGGAGTGAAATTGCA
1806
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 GAAGGAAAAGTCATTACTCGTGGTTTAGAGATAGTTAGGAGAGATTGGAGTGAAATTGCA
1860

Qy       1807 AAAGAAACTCAAGCTAGAGTTTTGGAGACAATACTAAAACACGGAGATGTTGAAGAAGCT
1866
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 AAAGAAACTCAAGCTAGAGTTTTGGAGACAATACTAAAACACGGAGATGTTGAAGAAGCT
1920
```

Table 1 continued

```
Qy       1867 GTGAGAATAGTAAAAGAAGTAATACAAAAGCTTGCCAATTATGAAATTCCACCAGAGAAG
1926

Db       1921 GTGAGAATAGTAAAAGAAGTAATACAAAAGCTTGCCAATTATGAAATTCCACCAGAGAAG
1980

Qy       1927 CTCGCAATATATGAGCAGATAACAAGACCATTACATGAGTATAAGGCGATAGGTCCTCAC
1986

Db       1981 CTCGCAATATATGAGCAGATAACAAGACCATTACATGAGTATAAGGCGATAGGTCCTCAC
2040

Qy       1987 GTAGCTGTTGCAAAGAAACTAGCTGCTAAAGGAGTTAAAATAAAGCCAGGAATGGTAATT
2046

Db       2041 GTAGCTGTTGCAAAGAAACTAGCTGCTAAAGGAGTTAAAATAAAGCCAGGAATGGTAATT
2100

Qy       2047 GGATACATAGTACTTAGAGGCGATGGTCCAATTAGCAATAGGGCAATTCTAGCTGAGGAA
2106

Db       2101 GGATACATAGTACTTAGAGGCGATGGTCCAATTAGCAATAGGGCAATTCTAGCTGAGGAA
2160

Qy       2107 TACGATCCCAAAAAGCACAAGTATGACGCAGAATATTACATTGAGAACCAGGTTCTTCCA
2166

Db       2161 TACGATCCCAAAAAGCACAAGTATGACGCAGAATATTACATTGAGAACCAGGTTCTTCCA
2220

Qy       2167 GCGGTACTTAGGATATTGGAGGGATTTGGATACAGAAAGGAAGACCTCAGATACCAAAAG
2226

Db       2221 GCGGTACTTAGGATATTGGAGGGATTTGGATACAGAAAGGAAGACCTCAGATACCAAAAG
2280

Qy       2227 ACAAGACAAGTCGGCCTAACTTCCTGGCTTAACATTAAAAAATCCGGTACCGGCGGTGGC
2286

Db       2281 ACAAGACAAGTCGGCCTAACTTCCTGGCTTAACATTAAAAAATCCGGTACCGGCGGTGGC
2340

Qy       2287 GGTGCAACCGTAAAGTTCAAGTACAAAGGCGAAGAAAAAGAGGTAGACATCTCCAAGATC
2346

Db       2341 GGTGCAACCGTAAAGTTCAAGTACAAAGGCGAAGAAAAAGAGGTAGACATCTCCAAGATC
2400
```

Table 1 continued

```
Qy       2347 AAGAAAGTATGGCGTGTGGGCAAGATGATCTCCTTCACCTACGACGAGGGCGGTGGCAAG
2406
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2401 AAGAAAGTATGGCGTGTGGGCAAGATGATCTCCTTCACCTACGACGAGGGCGGTGGCAAG
2460

Qy       2407 ACCGGCCGTGGTGCGGTAAGCGAAAAGGACGCGCCGAAGGAGCTGCTGCAGATGCTGGAG
2466
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2461 ACCGGCCGTGGTGCGGTAAGCGAAAAGGACGCGCCGAAGGAGCTGCTGCAGATGCTGGAG
2520

Qy       2467 AAGCAGAAAAAGTGA 2481
             ||||||||||||||||
Db       2521 AAGCAGAAAAAGTGA 2535
```

Application 10805650
Search Result 20061122_075011_us-10-805-650-127.gap0.1.rag.
Title: US-10-805-650-127
Perfect score: 4306
Sequence: 1 MILDVDYITEEGKPVIRLFK.....AVSEKDAPKELLQMLEKQKK 826

Amino Acid Match of SEQ ID NO. 8 to SEQ ID NO. 127 of instant application

```
RESULT 1
AAE15567
ID   AAE15567 standard; protein; 844 AA.
XX
AC   AAE15567;
XX
DT   29-AUG-2003  (revised)
DT   12-MAR-2002  (first entry)
XX
DE   Pyrococcus furiosus Pfu - Sulfolobus solfataricus Sso7d fusion protein.
XX
KW   Nucleic acid modifying enzyme; nucleic-acid-binding domain; Sac7d;
Sso7d;
KW   PolI DNA polymerase; Pfu DNA polymerase.
XX
OS   Pyrococcus furiosus.
OS   Sulfolobus solfataricus.
OS   Chimeric.
XX
PN   WO200192501-A1.
PD   06-DEC-2001.
PF   29-MAY-2001; 2001WO-US017492.
PR   26-MAY-2000; 2000US-0207567P.
PR   16-AUG-2000; 2000US-00640958.
```

Table 1 continued

PA (MJBI-) MJ BIOWORKS INC.
XX
PI **Wang Y;**
XX
DR WPI; 2002-075467/10.
DR N-PSDB; AAD24821.
XX
PT Protein for nucleic acid modification, consists of a heterologous
PT sequence-non-specific double-stranded nucleic-acid-binding domain joined
PT to a heterologous catalytic nucleic-acid-modifying domain.
XX
PS Example 1; **Page 48**; 65pp; English.
XX
CC The invention relates to improved generation of nucleic acid modifying
CC enzymes. The improvement is the fusion of a sequence-non-specificdouble-
CC stranded nucleic-acid-binding domain to the enzyme in a manner that
CC enhances the ability of the enzyme to bind and catalytically modify the
CC nucleic acid. The sequence-non-specific nucleic-acid-binding domain can
CC specifically bind to polyclonal antibodies generated against eitherSac7d
CC or Sso7d. Protein consisting of heterologous sequence-non-specificdouble
CC -stranded nucleic-acid-binding domain joined to heterologous catalytic
CC nucleic-acid-modifying domain is useful for modifying a nucleic acid in
CC an aqueous solution. The proteins of the invention are useful for
CC amplifying a subsequence of a target nucleic acid using a polymerase
CC chain reaction (PCR). The present sequence is Pyrococcus furiosus PolI
CC DNA polymerase (Pfu) - Sulfolobus solfataricus Sso7d fusion protein.
CC (Updated on 29-AUG-2003 to standardise OS field)
XX
SQ Sequence 844 AA;

Query Match 99.7%; Score 4294.2; DB 5; Length 844;
Best Local Similarity 97.9%; Pred. No. 1.8e-87;
Matches 826; Conservative 0; Mismatches 0; Indels 18; Gaps 1;

```
Qy          1 MILDVDYITEEGKPVIRLFKKENGKFKIEHDRTFRPYIYALLRDDSKIEEVKKITGERHG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MILDVDYITEEGKPVIRLFKKENGKFKIEHDRTFRPYIYALLRDDSKIEEVKKITGERHG 60

Qy         61 KIVRIVDVEKVEKKFLGKPITVWKLYLEHPQDVPTIREKVREHPAVVDIFEYDIPFAKRY
120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 KIVRIVDVEKVEKKFLGKPITVWKLYLEHPQDVPTIREKVREHPAVVDIFEYDIPFAKRY
120

Qy        121 LIDKGLIPMEGEEELKILAFDIETLYHEGEEFGKGPIIMISYADENEAKVITWKNIDLPY
180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 LIDKGLIPMEGEEELKILAFDIETLYHEGEEFGKGPIIMISYADENEAKVITWKNIDLPY
180
```

Table 1 continued

```
Qy       181 VEVVSSEREMIKRFLRIIREKDPDIIVTYNGDSFDFPYLAKRAEKLGIKLTIGRDGSEPK
240

Db       181 VEVVSSEREMIKRFLRIIREKDPDIIVTYNGDSFDFPYLAKRAEKLGIKLTIGRDGSEPK
240

Qy       241 MQRIGDMTAVEVKGRIHFDLYHVITRTINLPTYTLEAVYEAIFGKPKEKVYADEIAKAWE
300

Db       241 MQRIGDMTAVEVKGRIHFDLYHVITRTINLPTYTLEAVYEAIFGKPKEKVYADEIAKAWE
300

Qy       301 SGENLERVAKYSMEDAKATYELGKEFLPMEIQLSRLVGQPLWDVSRSSTGNLVEWFLLRK
360

Db       301 SGENLERVAKYSMEDAKATYELGKEFLPMEIQLSRLVGQPLWDVSRSSTGNLVEWFLLRK
360

Qy       361 AYERNEVAPNKPSEEEYQRRLRESYTGGFVKEPEKGLWENIVYLDFRALYPSIIITHNVS
420

Db       361 AYERNEVAPNKPSEEEYQRRLRESYTGGFVKEPEKGLWENIVYLDFRALYPSIIITHNVS
420

Qy       421 PDTLNLEGCKNYDIAPQVGHKFCKDIPGFIPSLLGHLLEERQKIKTKMKET---------
471

Db       421 PDTLNLEGCKNYDIAPQVGHKFCKDIPGFIPSLLGHLLEERQKIKTKMKETQDPIEKILL
480

Qy       472 ---------LANSFYGYYGYAKARWYCKECAESVTAWGRKYIELVWKELEEKFGFKVLYI
522

Db       481 DYRQKAIKLLANSFYGYYGYAKARWYCKECAESVTAWGRKYIELVWKELEEKFGFKVLYI
540

Qy       523 DTDGLYATIPGGESEEIKKKALEFVKYINSKLPGLLELEYEGFYKRGFFVTKKRYAVIDE
582

Db       541 DTDGLYATIPGGESEEIKKKALEFVKYINSKLPGLLELEYEGFYKRGFFVTKKRYAVIDE
600

Qy       583 EGKVITRGLEIVRRDWSEIAKETQARVLETILKHGDVEEAVRIVKEVIQKLANYEIPPEK
642

Db       601 EGKVITRGLEIVRRDWSEIAKETQARVLETILKHGDVEEAVRIVKEVIQKLANYEIPPEK
660
```

Table 1 continued

```
Qy        643 LAIYEQITRPLHEYKAIGPHVAVAKKLAAKGVKIKPGMVIGYIVLRGDGPISNRAILAEE
702
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 LAIYEQITRPLHEYKAIGPHVAVAKKLAAKGVKIKPGMVIGYIVLRGDGPISNRAILAEE
720

Qy        703 YDPKKHKYDAEYYIENQVLPAVLRILEGFGYRKEDLRYQKTRQVGLTSWLNIKKSGTGGG
762
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 YDPKKHKYDAEYYIENQVLPAVLRILEGFGYRKEDLRYQKTRQVGLTSWLNIKKSGTGGG
780

Qy        763 GATVKFKYKGEEKEVDISKIKKVWRVGKMISFTYDEGGGKTGRGAVSEKDAPKELLQMLE
822
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 GATVKFKYKGEEKEVDISKIKKVWRVGKMISFTYDEGGGKTGRGAVSEKDAPKELLQMLE
840

Qy        823 KQKK 826
              ||||
Db        841 KQKK 844
```

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Due to the rejections noted previously, the claims have been interpreted as follows for the applicability of prior art.

9. Claims 1-4, 7-11, 13, 15, 19, and 25-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang (WO 01/082501 published 2001), cited on the Information Disclosure Statement, IDS.

Regarding claims 1, 3, 25, 27, and 30, Wang teaches a method for cloning of a DNA synthesis product at high pH comprising:
a) providing a DNA polymerase fusion which is Pfu (wild type)-Sso7d (see p. 39, lines 13-16 for DNA polymerase fusion at high pH: "The reaction buffer for Pfu-Sso7d [fusion], Taq, and Sso7d-Taq was the above buffer [pH 8.8] . . ." and see Table 1 of this Office Action for sequence matching to wild type Pfu-protein Sso7d fusion); and
(b) contacting said fusion with a nucleic acid template, wherein said fusion permits DNA synthesis (see p. 39, line 6: "Lambda DNA (2.25 pM) was used as a PCR template").
c) inserting said synthesized DNA product into a cloning vector (see page lines "This nucleic acid can then be easily ligated into a vector containing a nucleic acid encoding the second domain and having the appropriate corresponding restriction sites").

Regarding claim 7, Wang teaches a method of linear or exponential PCR amplification at high pH for random mutagenesis comprising the steps of:
incubating a reaction mixture comprising a nucleic acid template, at least one PCR primers, and a DNA polymerase fusion under conditions which permit amplification of said nucleic acid template by said fusion to produce a mutated amplified product (for production of a mutated product see the teachings concerning Taq polymerase and fusion products prepared with it, see p. 10 lines 19-21: "However, because of the low

fidelity of such [Taq] polymerases, products cloned from such amplifications are likely to contain introduced mutations", and p. 35 lines 7-9: "*Unlike Taq polymerase*, Pfu possesses a 3' to 5' exonuclease activity, allowing it to maintain high fidelity during DNA synthesis", *emphasis* by Examiner).

Regarding claim 9, Wang teaches a method of reverse transcriptase PCR at high pH comprising the steps of

incubating a reaction mixture comprising a nucleic acid template, at least one PCR primer, and a DNA polymerase fusion under conditions which permit amplification of said nucleic acid template by said fusion to produce an amplified product (see p. 29, lines 12 and 13: "Similar assay conditions can be employed to test for improved processivity when the catalytic domain is a reverse transcriptase . . . ").

Although the "high pH" of claims 1, 3, 7, and 9 carries no patentable weight, as this is only recited in the preambles and not in the active steps, Wang does teach "high pH".

Regarding claims 2, 4, 8, and 10, Wang teaches a method comprising a PCR enhancing factor and/or an additive (see p. 39 lines 11-15 for additives and enhancing factors: "Each reaction contained 40 unit/ml of polymerase . . . and 0.36 mM of each of the four dNTPs. The reaction buffer used for Pfu (from Stratagene) contained 20 mM Tris-HCl (pH 8.8), 2 mM $MgSO_4$, 10 mM KCl, 10 mM $(NH4)_2SO_4$, 0.1% Triton X-100, and 0.1 mg/ml BSA").

Regarding claims 11 and 19, Wang teaches a method where the DNA polymerase fusion has reduced DNA polymerization activity (see p. 36, Table II where: PL-ΔTaq has <5% activity at 63°C which is less than the 85% activity of Taq at 63°C).

Regarding claims 13 and 15, Wang teaches a method where DNA polymerase fusion comprises reduced base analog detection activity (see p. 20, line 25-26: "In addition, nonclassical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the sequence").

Regarding claims 26 and 28, Wang teaches a method where a DNA polymerase fusion is a proofreading polymerase (see p. 2, lines 9 and 10: "These modified enzymes, e.g., Pfu-Sso7d, incorporate a polymerase with 10 error-correcting activity . . . ", and p. 6 line 28 and 29: " 'Error-correcting activity' of a polymerase or polymerase domain refers to the 3' to 5' exonuclease proofreading activity of a template-specific nucleic acid polymerase . . .", and p. 38 lines 27 and 28: "As demonstrated in Example 2, Sso7d fusion proteins have significantly higher processivity than their unmodified counterparts").

Regarding claims 29, Wang teaches a method where a DNA polymerase fusion further comprises a polypeptide with a reduced extension time in a PCR reaction (see p. 2 lines 12-14: "In addition, such modified enzymes can efficiently amplify a given fragment using shorter extension times than are required by conventional polymerase mixtures").

10. Claims 1-10, 13, 25, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Gelfand et al. (U.S. Patent No. 4,889,818, issued December 26, 1989), cited on the IDS.

Gelfand et al. disclose a fusion DNA polymerase and a reagent buffer at pH around 8 to 8.4, which is considered high (column 3, lines 58-61; column 8, lines 12-17). The artisans also disclose the use of $MgCl_2$ which is known in the art to enhance polymerase chain reaction (column 3, line 59).

Gelfand et al. disclose a method of performing amplification and nucleic acid sequencing reaction, employing said DNA polymerase fusion (column 2, lines 16-27), primers (column 3, lines 47-56). The polymerase fusion of Gelfand et al. is heat stable (column 2, lines 40-53). Therefore, Gelfand et al. anticipate the invention as claimed.

11. Claims 1-11, 26, 28, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Dahlberg et al. (U.S. Patent No. 5,541,31 I, issued July 30, 1996), cited on the IDS.

Dahlberg et al. disclose a DNA polymerase fusion comprising a reduced DNA polymerization activity (column 15, lines 42-45), used in a method of amplification and sequencing reactions (column 16, lines 30-32).

Therefore the Dalhberg et al. anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (2001) as applied to claims 1-4, 7-11, 13, 15, 19, and 25-30 above, and further in view of Sanger et al. (1977).

Wang teaches as noted above, including the PCR additives recited in claim 6.

Wang does not specifically teach chain-terminating nucleotide analogs recited in claim 5.

Sanger et al. teach 2',3'-dideoxythymidine triphosphate (ddTTP) which is a chain-terminating nucleotide analog in a method using DNA polymerase for DNA Sequencing (see p. 5463, 1st sentence under the section *Principle of the Method* and Title).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the polymerase fusion method of Wang by using a chain-terminating nucleotide analog as suggested by Sanger with a reasonable expectation of success. The motivation to do so is provided by Wang who teaches: "The modifying proteins [including polymerase fusions] that are processive in nature exhibit increased processivity when joined to a binding domain compared to the enzyme alone" (see p. 1, 3rd paragraph, 4th sentence). In other words, Wang teaches

that a polymerase fusion may be substituted for the polymerase itself in any method using a polymerase, including that of Sanger et al., and that this substitution is beneficial. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

13. No elected claim is free of the prior art.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples
Examiner
Art Unit 1637
December 5, 2006

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
12/6/06